

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

1. (original) A pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease comprising a sugar-modified liposome having a sugar chain bound to the membrane of the liposome.

2. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 1, wherein lipids constituting the liposome comprise phosphatidylcholines (at a molar ratio of 0 to 70%), phosphatidylethanolamines (at a molar ratio of 0 to 30%), one or more lipids (at a molar ratio of 0 to 30%) selected from the group consisting of phosphatidic acids, long-chain alkyl phosphates, and dicetylphosphoric acids, one or more lipids (at a molar ratio of 0 to 40%) selected from the group consisting of gangliosides, glycolipids, phosphatidylglycerols, and sphingomyelins, and cholesterol (at a molar ratio of 0 to 70%).

3. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 2, wherein at least one lipid selected from the group consisting of gangliosides, glycolipids, phosphatidylglycerols, sphingomyelins, and cholesterol assembles to form a raft on the surface of the liposome.

4. (currently amended) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to ~~any one of claims 1 to 3~~ claim 1, wherein the sugar chain is bound to the membrane of the liposome in a manner that controls the type and density of the sugar chain.

5. (currently amended) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to ~~any one of claims 1 to 4~~ claim 1, wherein the liposome has a particle size of 30 to 500 nm.

6. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 5, wherein the liposome has a particle size of 50 to 300 nm.

7. (currently amended) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to ~~any one of claims 1 to 6~~ claim 1, wherein the liposome has a zeta potential of -50 to 10 mV.

8. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 7, wherein the liposome has a zeta potential of -40 to 0 mV.

9. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 8, wherein the liposome has a zeta potential of -30 to -10 mV.

10. (currently amended) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to any one of ~~claims 1 to 9~~ claim 1, wherein the sugar chain is bound to the membrane of the liposome through a linker protein.

11. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 10, wherein the linker protein is an organism-derived protein.

12. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 11, wherein the linker protein is a human-derived protein.

13. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 12, wherein the linker protein is a human-derived serum protein.

14. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 10, wherein the linker protein is human serum albumin or bovine serum albumin.

15. (currently amended) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to ~~any one of claims 1 to 14~~ claim 1, wherein the linker protein is bound to the raft consisting of at least one lipid selected from the group consisting of gangliosides, glycolipids, phosphatidylglycerols, sphingomyelins, and cholesterol, formed on the surface of the liposome.

16. (currently amended) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to ~~any one of claims 1 to 15~~ claim 1, wherein the pharmaceutical composition is hydrophilized by bonding a hydrophilic compound to the membrane of the liposome and/or the linker protein.

17. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 16, wherein the hydrophilic compound is a substance having a low molecular weight.

18. (currently amended) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 16 ~~or 17~~, wherein the hydrophilic

compound is less apt to sterically hinder the sugar chain and does not prevent lectin on the membrane surface of a target cell from proceeding reaction of recognizing the sugar-chain molecule.

19. (currently amended) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to ~~any one of claims 16 to 18~~ claim 16, wherein the hydrophilic compound has a hydroxyl group.

20. (currently amended) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to ~~any one of claims 16 to 19~~ claim 16, wherein the hydrophilic compound is any of amino alcohols.

21. (currently amended) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to ~~any one of claims 16 to 20~~ claim 16, wherein the hydrophilic compound is directly bonded to the membrane surface of the liposome.

22. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 16 which is a sugar-modified liposome, wherein the pharmaceutical composition is hydrophilized with a hydrophilic compound represented by the general formula (1):

X-R₁(R₂OH)_n (1)

wherein R₁ represents a C₁₋₄₀ linear or branched hydrocarbon chain; R₂ is absent or represents a C₁₋₄₀ linear or branched hydrocarbon chain; X represents a reactive functional group bonded either directly to the lipid of the liposome or the linker protein or to a bivalent crosslinking reagent; and n represents a natural number.

23. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 16 which is a sugar-modified liposome, wherein the pharmaceutical composition is hydrophilized with a hydrophilic compound represented by the general formula (2):

H₂N-R₃-(R₄OH)_n (2)

wherein R₃ represents a C₁₋₄₀ linear or branched hydrocarbon chain; R₄ is absent or represents a C₁₋₄₀ linear or branched hydrocarbon chain; H₂N represents a reactive functional group bonded either directly to the lipid of the liposome or the linker protein or to a bivalent crosslinking reagent; and n represents a natural number.

24. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 16 which is a sugar-modified liposome, wherein the pharmaceutical composition is hydrophilized with a hydrophilic compound represented by the general formula (3):

$\text{H}_2\text{N}-\text{R}_5(\text{OH})_n$ (3)

wherein R_5 represents a C_{1-40} linear or branched hydrocarbon chain; H_2N represents a reactive functional group bonded, either directly to the lipid of the liposome or the linker protein or to a bivalent crosslinking reagent; and n represents a natural number.

25. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 16, wherein the membrane of the liposome and/or the linker protein are hydrophilized by covalently bonding a hydrophilic compound that is tris(hydroxyalkyl)aminoalkane to the membrane of the liposome and/or the linker protein.

26. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 16, wherein the membrane of the liposome and/or the linker protein are hydrophilized by covalently bonding a hydrophilic compound selected from the group consisting of tris(hydroxymethyl)aminoethane, tris(hydroxyethyl)aminoethane, tris(hydroxypropyl)aminoethane, tris(hydroxymethyl)aminomethane, tris(hydroxyethyl)aminomethane, tris(hydroxymethyl)aminopropane, tris(hydroxyethyl)aminopropane, and tris(hydroxypropyl)aminopropane to the membrane of the liposome and/or the linker protein.

27. (currently amended) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to any one of claims 1 to 26 claim 1, wherein

the sugar-modified liposome targets lectin selected from the group consisting of C-type lectin comprising selectin, DC-SIGN, DC-SGNR, collectin, and mannose-binding lectin, I-type lectin comprising siglec, P-type lectin comprising a mannose-6-phosphate receptor, R-type lectin, L-type lectin, M-type lectin, and galectin, which serves as a receptor residing on the cell-membrane surface of each tissue.

28. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 27, wherein the sugar-modified liposome targets selectin selected from the group consisting of E-selectin, P-selectin, and L-selectin.

29. (currently amended) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to any ~~one of claims 1 to 28~~ claim 1, wherein the sugar chain is bound to the liposome at a density of 1 to 60 sugar chains per linker protein molecule bound to the liposome.

30. (currently amended) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to any ~~one of claims 1 to 28~~ claim 1, wherein the sugar chain is bound to the liposome at a density of 1 to 30000 sugar chains per liposome molecule in the case of using the linker protein, and at a maximum density of 1 to 500000 sugar chains per liposome molecule in the case of not using the linker protein.

31. (currently amended) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to ~~any one of claims 1 to 30~~ claim 1, wherein the sugar chain is selected from the group consisting of Lewis X trisaccharide, sialyl Lewis X tetrasaccharide, 3'-sialyllactosamine trisaccharide, 6'-sialyllactosamine trisaccharide, α -1,2-mannobiose disaccharide, α -1,3-mannobiose disaccharide, α -1,4-mannobiose disaccharide, α -1,6-mannobiose disaccharide, α -1,3/ α -1,6-mannotriose trisaccharide, oligomannose-3 pentasaccharide, oligomannose-4b hexasaccharide, oligomannose-5 heptasaccharide, oligomannose-6 octasaccharide, oligomannose-7 nonasaccharide, oligomannose-8 decasaccharide, oligomannose-9 undecasaccharide, lactose disaccharide, 2'-fucosyllactose trisaccharide, difucosyllactose tetrasaccharide, 3-fucosyllactose trisaccharide, 3'-sialyllactose trisaccharide, and 6'-sialyllactose trisaccharide.

32. (currently amended) The pharmaceutical composition for the medical treatment of an inflammatory disease according to ~~any one of claims 1 to 31~~ claim 1, wherein the sugar-modified liposome comprises a drug selected from the group consisting of adrenocortical hormones, antiinflammatory drugs, immunosuppressive drugs, anticancer drugs, antimicrobial drugs, antiviral drugs, angiogenesis inhibitors, cytokines, chemokines, anti-cytokine antibodies, anti-chemokine antibodies, anti-cytokine/chemokine receptor antibodies, nucleic acid preparations for therapy using genes such as siRNA and DNA, neuroprotective factors, and antibody drugs.

33. (original) The pharmaceutical composition for the medical treatment of an inflammatory disease according to claim 32, wherein the sugar-modified liposome comprises an adrenocortical hormone or an antiinflammatory drug as the drug.

34. (original) The pharmaceutical composition for the medical treatment of an inflammatory disease according to claim 33, wherein the sugar-modified liposome comprises prednisolone as the drug.

35. (currently amended) The pharmaceutical composition for the medical treatment of an inflammatory disease according to any one of claims 32 to 34 claim 32 , wherein the drug can be accumulated in an inflammatory site at a level 10 or more times higher than that of the drug administered alone.

36. (currently amended) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to any one of claims 1 to 35 claim 1 , wherein the inflammatory disease is selected from the group consisting of encephalitis, inflammatory eye disease, otitis, pharyngitis, pneumonia, gastritis, enteritis, hepatitis, pancreatitis, nephritis, cystitis, urethritis, endometritis, vaginitis, arthritis, peripheral neuritis, malignant tumor, infectious diseases, autoimmune diseases such as rheumatism, systemic lupus erythematosus, and sarcoidosis, ischemic diseases such as myocardial infarction and cerebral infarction,

metabolic diseases such as diabetes and gout, injury, scald, chemical corrosion, and neurodegenerative diseases such as Alzheimer's disease.

37. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 36, wherein the inflammatory disease is inflammatory eye disease.

38. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 36, wherein the inflammatory disease is rheumatism.

39. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 36, wherein the inflammatory disease is enteritis.

40. (currently amended) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to ~~any one of claims 1 to 39~~ claim 1, wherein the pharmaceutical composition is a pharmaceutical composition for oral administration.

41. (currently amended) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to ~~any one of claims 1 to 39~~ claim 1, wherein the pharmaceutical composition is a pharmaceutical composition for parenteral administration.

42. (original) A pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease comprising a liposome having a hydrophilized membrane surface to which no sugar chain is bound.

43. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 42, wherein lipids constituting the liposome comprise phosphatidylcholines (at a molar ratio of 0 to 70%), phosphatidylethanolamines (at a molar ratio of 0 to 30%), one or more lipids (at a molar ratio of 0 to 30%) selected from the group consisting of phosphatidic acids, long-chain alkyl phosphates, and dicetylphosphoric acids, one or more lipids (at a molar ratio of 0 to 40%) selected from the group consisting of gangliosides, glycolipids, phosphatidylglycerols, and sphingomyelins, and cholesterols (at a molar ratio of 0 to 70%).

44. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 43, wherein the liposome further comprises a protein.

45. (currently amended) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to any one of claims 42 to 44 claim 42,

PRELIMINARY AMENDMENT

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wherein the pharmaceutical composition is hydrophilized by bonding a hydrophilic compound to the membrane of the liposome and/or the linker protein.

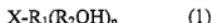
46. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 45, wherein the hydrophilic compound is a substance having a low molecular weight.

47. (currently amended) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 45 or 46, wherein the hydrophilic compound has a hydroxyl group.

48. (currently amended) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to any one of claims 45 to 47 claim 45, wherein the hydrophilic compound is any of amino alcohols.

49. (currently amended) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to any one of claims 45 to 48 claim 45, wherein the hydrophilic compound is directly bonded to the membrane surface of the liposome.

50. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 45, wherein the pharmaceutical composition is hydrophilized with a hydrophilic compound represented by the general formula (1):



wherein R₁ represents a C₁₋₄₀ linear or branched hydrocarbon chain; R₂ is absent or represents a C₁₋₄₀ linear or branched hydrocarbon chain; X represents a reactive functional group bonded either directly to the lipid of the liposome or the linker protein or to a bivalent crosslinking reagent; and n represents a natural number.

51. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 45, wherein the pharmaceutical composition is hydrophilized with a hydrophilic compound represented by the general formula (2):



wherein R₃ represents a C₁₋₄₀ linear or branched hydrocarbon chain; R₄ is absent or represents a C₁₋₄₀ linear or branched hydrocarbon chain; H₂N represents a reactive functional group bonded either directly to the lipid of the liposome or the linker protein or to a bivalent crosslinking reagent; and n represents a natural number.

52. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 45, wherein the pharmaceutical composition is hydrophilized with a hydrophilic compound represented by the general formula (3):



wherein R_5 represents a C_{1-40} linear or branched hydrocarbon chain; H_2N represents a reactive functional group bonded either directly to the lipid of the liposome or the linker protein or to a bivalent crosslinking reagent; and n represents a natural number.

53. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 45, wherein the membrane of the liposome and/or the linker protein are hydrophilized by covalently bonding a hydrophilic compound that is tris(hydroxyalkyl)aminoalkane to the membrane of the liposome and/or the linker protein.

54. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 53, wherein the membrane of the liposome and/or the linker protein are hydrophilized by covalently bonding a hydrophilic compound selected from the group consisting of tris(hydroxymethyl)aminoethane, tris(hydroxyethyl)aminoethane, tris(hydroxypropyl)aminoethane, tris(hydroxymethyl)aminomethane, tris(hydroxyethyl)aminomethane, tris(hydroxypropyl)aminomethane, tris(hydroxymethyl)aminopropane, tris(hydroxyethyl)aminopropane, and tris(hydroxypropyl)aminopropane to the membrane of the liposome and/or the linker protein.

55. (currently amended) The pharmaceutical composition for the medical treatment of an inflammatory disease according to ~~any one of claims 42 to 54~~ claim 42, wherein the liposome comprises a drug selected from the group consisting of adrenocortical hormones, antiinflammatory drugs, immunosuppressive drugs, anticancer drugs, antimicrobial drugs, antiviral drugs, angiogenesis inhibitors, cytokines, chemokines, anti-cytokine antibodies, anti-chemokine antibodies, anti-cytokine/chemokine receptor antibodies, nucleic acid preparations for therapy using genes such as siRNA and DNA, neuroprotective factors, and antibody drugs.

56. (original) The pharmaceutical composition for the medical treatment of an inflammatory disease according to claim 55, wherein the liposome comprises an adrenocortical hormone or an antiinflammatory drug as the drug.

57. (original) The pharmaceutical composition for the medical treatment of an inflammatory disease according to claim 56, wherein the liposome comprises prednisolone as the drug.

58. (currently amended) The pharmaceutical composition for the medical treatment of an inflammatory disease according to ~~any one of claims 55 to 57~~ claim 55, wherein the drug can be accumulated in an inflammatory site at a level 10 or more times higher than that of the drug administered alone.

59. (currently amended) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to ~~any one of claims 42 to 58~~ claim 42, wherein the inflammatory disease is selected from the group consisting of encephalitis, inflammatory eye disease, otitis, pharyngitis, pneumonia, gastritis, enteritis, hepatitis, pancreatitis, nephritis, cystitis, urethritis, endometritis, vaginitis, arthritis, peripheral neuritis, malignant tumor, infectious diseases, autoimmune diseases such as rheumatism, systemic lupus erythematosus, and sarcoidosis, ischemic disease such as myocardial infarction and cerebral infarction, metabolic diseases such as diabetes and gout, injury, scald, chemical corrosion, and neurodegenerative disease such as Alzheimer's disease.

60. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 59, wherein the inflammatory disease is inflammatory eye disease.

61. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 59, wherein the inflammatory disease is rheumatism.

62. (original) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to claim 59, wherein the inflammatory disease is enteritis.

63. (currently amended) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to ~~any one of claims 42 to 62~~ claim 42, wherein the pharmaceutical composition is a pharmaceutical composition for oral administration.

64. (currently amended) The pharmaceutical composition for the medical treatment or diagnosis of an inflammatory disease according to ~~any one of claims 42 to 62~~ claim 42, wherein the pharmaceutical composition is a pharmaceutical composition for parenteral administration.